Epitomes

Important Advances in Clinical Medicine

Urology

Daniel A. Nachtsheim, MD, Section Editor

The Council on Scientific Affairs of the California Medical Association presents the following epitomes of progress in urology. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, as to both scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, and scholars to stay abreast of these items of progress in urology that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Urology of the California Medical Association, and the summaries were prepared under the direction of Dr Nachtsheim and the Panel.

Best Screening Tests for Prostate Cancer

IN 1998 ALONE, about 500 men will be diagnosed with prostate cancer every day, and approximately 39,000 will die of the disease. Recognizing that population screening for prostate cancer using PSA and DRE have neither been proven or disproven to be effective to reduce the morbidity and mortality of the disease, authorities now recommend that physicians and health care organizations provide the pros and cons and let the well-informed patient decide. Just as it would be wrong to mandate screening, it would be just as wrong to not offer the option of early detection tests for prostate cancer.

Potential screening tests for prostate cancer include the digital rectal exam (DRE), the seromarkers prostate specific antigen (PSA) and prostatic acid phosphatase (PAP), and transrectal ultrasound of the prostate (TRUS). The DRE remains an important method of detecting many prostate cancers that may be missed with a PSA test. The PSA test is a simple blood test. Although PSA and PAP are both seromarkers for prostate cancer, the latter is inappropriate for use in screening because levels of PAP often do not become elevated until the disease has reached an advanced stage. Therefore, PAP should be used only for staging the disease after it has been diagnosed and never for screening. Transrectal ultrasound of the prostate is not a suitable screening test. It cannot differentiate many small cancers from surrounding non-cancerous prostate tissue, but it is appropriate for directing biopsies in men who have abnormal findings on DRE or PSA testing.

The PSA test has been approved by the US Food and Drug Administration as a method of screening for prostate cancer, but it is not perfect. Although a PSA level > 4.0 ng/ml is considered abnormal, men with a level of between 4.1 and 10.0 ng/ml, often considered the "grey zone," will have prostate cancer detected about one-third of the time. In men with a PSA level >10.0 ng/ml, approximately two-thirds will have cancer. The specificity is only 59% for all PSA levels >4.0 ng/ml. Sensitivity is also suboptimal, as levels >4.0 ng/ml will detect prostate cancer in only 79% of cases. In other words, the use of this cutoff point will miss 21% of patients with prostate cancer who have PSA levels of <4.0 ng/ml.

Several recent refinements may improve the clinical utility of PSA. Measurements of PSA density are based on the ratio between the PSA level and the prostate volume (as measured on transrectal ultrasound). A PSA density value less than 0.15 in a patient suggests that benign prostatic hypertrophy (BPH) alone may be responsible for the PSA elevation and a biopsy may not be indicated if the digital rectal examination is normal. This method helps adjust for the proportion of PSA elevation that may be related simply to BPH. However, the reliability of the method depends on reproducible measurements of prostate volume by transrectal ultrasound.

Assessments of PSA rate of change or PSA velocity are useful for men who undergo screening over a period of time. A PSA increase >0.75–0.80 ng/ml over a one-year period may indicate an increased probability of prostate cancer and may signal the need for further evaluation. On the other hand, recent research has suggested that men who start with a very low PSA value less than 2.0 ng/ml have a very low probability of jumping to a worrisome PSA over one year and that every-other-year testing may be acceptable for this group. Some, but not all studies have suggested that digital rectal examination, ejaculation, or bicycle riding may raise the PSA level unrelated to prostate cancer leading to a false positive test. In a man with mildly elevated PSA level, these things should be avoided for 48–72 hours prior to repeat testing.

Recently, the use of age-specific reference ranges (ASRRs) has generated particular interest. These ranges,

derived from control populations of men without prostate cancer, adjust for the increases in prostatic hyperplasia and PSA levels that occur with aging. Levels above the 95th percentile of these normal men by decade of age are considered abnormal. Newer data have suggested that different racial groups may have different ASRRs. For instance, ASRRs are lower in Japanese men than in American men. Also, African American men with newly diagnosed prostate cancer have higher serum PSA values than do whites, even after correction for stage, grade, and tumor volume.

Aside from PSA-density, rate-of-change and ASRR, another tool—the "free" PSA—has recently been FDA-approved. Over the last few years, researchers discovered that PSA protein may be free or bound to other proteins in the bloodstream. Most PSA is complexed to other proteins, most commonly a protein called alpha-1 antichymoltrypsin (ACT). The percentage of free, complexed and total PSA and their ratios are different between men who do and do not have prostate cancer and these differences can be exploited to screen for prostate cancer. The most useful ratio identified to date is the percentage of free PSA to the total PSA. Although studies are still being conducted, it appears that the lower the percent of free PSA, the higher the risk of prostate cancer.

With the aging of the U.S. population and the high incidence of prostate cancer, the debate regarding the early detection of the disease continues. Although randomized clinical trials have yet to prove or disprove the efficacy of prostate cancer population-based screening, patients should be counseled regarding the pros and cons of early detection. The PSA and DRE tests are accepted case finding tools. Many urologists favor a strategy of annual PSA blood tests and DREs for men >50 years old. Annual assessments should begin at age 40 for African American men and those who have a family history of prostate cancer. New "PSA-tools" such as age- and race-specific reference ranges and free-PSA seem to make the testing more reliable. The relationships between testing, treatment, and outcome need further clarification.

JUDD W. MOUL, MD
Bethesda, Maryland

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Urolithiasis

RENAL AND URETERAL stones are frequently encountered In industrialized countries, in contrast to bladder calculi noted in developing countries and ancient times. Most ureteral calculi are passed spontaneously. Extracorporeal shock wave lithotripsy (ESWL), ureteroscopy, and percutaneous nephrolithotomy are saved for patients in whom spontaneous passage has failed. Dietary modifications and medical treatment can reduce recurrent urinary stone disease substantially. Despite improved surgical treatment, 50% of patients will have recurrent stones within 5 years if no metabolic intervention is undertaken.

Patients usually present with acute flank pain associated with nausea and vomiting. Chronic back pain, hematuria and incidental discovery with radiographic imaging are other frequent reasons for referral to urinary stone centers. Eighty-five percent of patients with urinary calculi will have either micro or gross hematuria. A complete blood count is warranted for patients who have calculi and fever. Serum electrolytes and creatinine should be obtained. A plain abdominal radiograph (KUB) is the best initial imaging modality; it helps pinpoint the location of the calculus, since 85-90% of urinary tract calculi are radio-opaque. The KUB may be followed by directed renal sonography or intravenous pyelography to confirm stone location and guide management. Where available, non-contrast helical CT scanning is becoming the examination of choice for acute renal colic. It is safe, rapid, and has shown 97% sensitivity and 96% specificity in detecting renal and ureteral calculi.

Acute renal colic is treated initially with analgesics and hydration to maintain a euvolemic state. The majority of ureteral calculi less than 6 mm in size will pass with this management. Pain, persistent vomiting, fever, or failure of stone progression requires intervention.

A medical evaluation for patients who form stones more than once should be initiated after the acute stone episode is resolved. The stone should be retrieved and analyzed. Serum electrolytes, creatinine, calcium, phosphate, uric acid, and parathyroid hormone (PTH) should be obtained. A 24-hour urine collection including urine volume, pH, specific gravity, calcium, creatinine, citrate, oxalate, phosphate, uric acid, and sodium will direct medical therapy.

Stone analysis, revealing either calcium or non-calcium calculi, guides medical management. Most stones are composed of calcium oxalate. Pure calcium phosphate calculi may indicate the presence of distal renal tubular acidosis (RTA) or primary hyperparathyroidism. Hypokalemia and decreased serum bicarbonate with a fasting urinary pH > 5.5 confirms the diagnosis of distal RTA (type1). Elevated serum PTH, calcium and decreased serum phosphorus characterize patients with primary hyperparathyroidism.

Calcium urolithiasis can be subdivided into hypercalciuric and normocalciuric states. The hypercalciuric metabolic defects may be sub-classified as absorptive, resorptive and "renal leak".

There are 3 classes of absorptive hypercalciuria: diet independent (type I), diet dependent (type II), and renal phosphate leak (type III). All are characterized by >250 mg. of calcium in a 24 hour urine specimen. Type I